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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Sampson, J.	Art Unit:	1635
Serial No.:	09/358,141	Examiner:	Schmidt, M.
Filed:	July 20,1999		
For:	METHOD OF PRODUCING NUCLEIC ACID MOLECULES WITH REDUCED SECONDARY STRUCTURE		

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, DC 20231
Sir:

REQUEST FOR RECONSIDERATION OF REQUIREMENT

UNDER 37 C.F.R. §1.143

The present patent application describes and claims methods of synthesizing nucleic acids that preferentially form intermolecular rather than intramolecular base pair interactions, and names these nucleic acids "unstructured nucleic acids" (UNAs). The application demonstrates for the first time that it is possible to select collections of nucleotides and/or nucleotide analogs that can be used in extension reactions to generate such UNAs.

A Restriction Requirement was issued in the case (Paper Number 19, mailed May 8, 2002), asserting that methods utilizing different categories of polymerases are patentably distinct from one another. In Response to that Restriction Requirement, Applicant elected claims to RNA Polymerases. The Examiner has now issued an Election Requirement, asserting that it would be unduly burdensome to search more than one RNA Polymerase at a time to determine which nucleotide analogs have been used with which RNA Polymerase.

Applicant respectfully disagrees. Moreover, Applicant asserts that a strategy of individually searching RNA Polymerases to identify the universe of references mentioning nucleotide analogs used with those RNA Polymerases would be unproductive as both unduly

broad and unduly narrow. The present invention establishes that it is possible to define sets of nucleotides and nucleotide analogs that can preferentially form intermolecular interactions, and then defines representative sets. In light of the inventive teachings, those of ordinary skill in the art can readily test various combinations of nucleotides and/or analogs with various polymerases to define other sets that can appropriately be used in accordance with the present invention. However, absent the inventive recognition that such sets are desirable and can be developed, those of ordinary skill in the art would not and could not have defined them. A search limited by RNA polymerase would identify too many references because it would identify any reference using that polymerase with any nucleotide or nucleotide analog. The search would simultaneously identify too few references because it would not identify references that might utilize relevant sets of nucleotides with other polymerases. Applicant respectfully submits that a single search for nucleotides that preferentially form intermolecular base pairs would appropriately define the literature relevant to the present invention, regardless of the particular polymerase being employed in a given reaction.

Applicant further notes that researchers have recently begun to recognize the value of defining nucleotide sets as described by the present invention. For example, Nguyen and Southern have recently (after the filing date of the present application) published a paper (Nguyen, H-G. and Southern E. M., (2000) *Nucleic Acid Research*, 28 3904-3909 (Exhibit A)), that describes "a *new* strategy for minimizing the secondary structure in the target DNA by introduction of modified nucleotides into the target that form weak base pairs" (emphasis added); pg. 3904, column 2, lines 4-8). These authors recognized that the approach of defining sets of nucleotides with reduced ability to interact intramolecularly is new, and further immediately appreciated its generality ("Base substitutions in the target and/or probe would be a simple,

potentially general method to overcome the problem...."; page 3909, column 1, lines 12-14). Nguyen and Southern did not consider the strategy to be limited to any particular polymerase.

For all of these reasons, Applicant respectfully requests withdrawal of the Election Requirement. Should the Examiner refuse to withdraw the requirement, Applicant requests that the search be initiated for the T7 polymerase. Please charge any fees that may be associated with this matter, or credit any overpayments, to our Deposit Account No. 50-1078.

Respectfully submitted,

Dated: 10/8/2002

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